A Response to the Office Action Dated August 27, 2003:

A. Status of the Claims

Claims 28, 29, and 37-54 were pending at the time the Action was issued on August 27, 2003. Claims 28, 42, and 49 have been amended. Support for these amendments can be found throughout the specification and claims as originally filed. *See, e.g*, the specification at page 40, lines 17-20. No new matter has been added by these amendments. Claims 28, 29, and 37-54, therefore, are currently pending.

B. The Written Description Rejection is Overcome

The Action rejects claims 42-48 under 35 U.S.C. § 112, first paragraph, by contending that the specification does not contain a written description of the claimed invention. Specifically, the Action states that the term "is not a phosphatidylserine/KLH conjugate composition" has no written description support in the specification.

Applicant traverses this rejection. Claims 42-48 satisfy all of the requirements of 35 U.S.C. § 112, first paragraph.

As an initial matter, Applicant notes that it is settled law that negative limitations in claims are allowable. *See, e.g., Manuel of Patent Examining Procedure* (MPEP) § 2173.05(i), 8th Ed. Rev. 1, Feb. 2003 ("The current view of the courts is that there is nothing inherently ambiguous or uncertain about a negative limitation."). More specifically, a negative limitation in a claim that disclaims one embodiment of an invention does not create a written description issue. *Id.* ("If alternative elements are positively recited in the specification, ***they may be explicitly excluded in the claims***.") (emphasis added); *see also, In re Johnson and Farnham*, 194 U.S.P.Q. 187, 196 (C.C.P.A. 1977) ("Here, as we hold on the facts of this case, the 'written

description' in the 1963 specification supported the claims in the absence of the limitation, and that specification, having described the whole, necessarily described the part remaining.").

Applicant's specification and claims as originally filed more than adequately describes a phosphatidylserine/KLH conjugate composition. *See, e.g.*, the specification at page 5, lines 12-20. Because a phosphatidylserine/KLH conjugate composition is positively recited in the specification, Applicant can explicitly exclude such a composition from the claims. *See* MPEP § 2173.05(i). As such, the present written description rejection cannot be maintained.

Accordingly, Applicant requests that the written description rejection of claims 42-48 under 35 U.S.C. § 112, first paragraph, be withdrawn.

C. The Anticipation Rejections Are Overcome

1. Claims 28-29, 38, 42-43, and 45 are not anticipated by Tamamura *et al.*

i. A summary of the rejection and Applicant's claimed invention

The Action rejects claims 28-29, 38, 42-43, and 45 under 35 U.S.C. § 102(b) as being anticipated by Tamamura *et al.* (Tamamura). Specifically, the Action contends that Tamamura discloses a method of administering to an animal an immunologically effective amount of a mixture having phosphatidylserine (PS) and methylated bovine serum albumin (MBSA) to elicit antibodies that specifically bind to phosphatidylserine. From this, the Action concludes that the PS and the MBSA are "conjugate[d]" together.

Applicant traverses this rejection. Claims 28-29, 38, 42-43, and 45 are not anticipated by Tamamura.

Anticipation requires that each and every element of the claimed invention be described, either expressly or inherently, in a single prior art reference. *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316, 1327, 58 U.S.P.Q.2d 1545, 1552 (Fed. Cir. 2001); *Verdegaal*

Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). It is well settled that the burden of establishing a *prima facie* case of anticipation resides with the Examiner and only if that burden is met, does the burden of going forward shift to the applicant. *See In re Sun*, 31 U.S.P.Q.2d 1451 (Fed. Cir. 1993).

Applicant presently claims "[a] method of making an antibody that specifically binds to phosphatidylserine, said method comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of a phosphatidylserine/polypeptide conjugate composition, ***wherein the phosphatidylserine is covalently coupled to the polypeptide.*** (claim 28) (emphasis added). In particular aspects, the antibody can be a monoclonal antibody (claims 41 and 48-54). In other embodiments, "the phosphatidylserine/polypeptide conjugate composition is not a phosphatidylserine/KLH conjugate composition" (claim 42).

ii. Tamamura does not teach or suggest a phosphatidylserine/polypeptide conjugate composition wherein the phosphatidylserine is covalently coupled to the polypeptide

In contrast to Applicant's claimed invention, the Tamamura reference is directed towards a mixture having PS and MBSA. *See* Tamamura, page 32. In this regard, Tamamura states that "[t]he equal volume of 0.1% MBSA solution was ***mixed*** with the lipid emulsion resulting with a white cloudy suspension." *Id.* (emphasis added). Tamamura does not appear to include any teachings of covalently coupling the PS with the MBSA. In fact, the Action appears to admit this much. *See* the Action, page 4.

Because Tamamura fails to teach or suggest a phosphatidylserine/polypeptide conjugate composition wherein the phosphatidylserine is covalently coupled to the polypeptide, it does not teach each and every element of the present invention. As such, the present anticipation rejection cannot be maintained.

Accordingly, Applicant requests that the rejection of claims 28-29, 38, 42-43, and 45 as being anticipated by Tamamura be withdrawn.

iii. Tamamura fails to teach or suggest a method of making a monoclonal antiboby

Claims 41 and 48-54 are further patentable over the Tamamura reference because this reference fails to teach or suggest a method of making a monoclonal antibody, much less a monoclonal antibody that specifically binds to phosphatidylserine. In Tamamura, the collaborators produced antisera by intravenously injecting a mixture having PS and MBSA into rabbits. *See* Tamamura, page 32. As stated by Tamamura, "[t]he inoculation [sic] were repeated three times a week, and injections were given to each animal. The animals were sacrificed 10 days after last inoculation." *Id.* A person of ordinary skill in the art would understand that this procedure does not produce monoclonal antibodies. *See, e.g.*, the specification, page 14, line 16, to page 15, line 10.

By contrast, claims 41 and 48-54 are specifically directed towards methods of producing a monoclonal antibody. Because Tamamura does not teach or suggest a method of making a monoclonal antibody, it does not teach every element of the present invention. As such, claims 41 and 48-54 are further not anticipated by this reference.

2. Claims 28, 38-40, 42, and 45-47 are not anticipated by Maneta-Peyret *et al.*

i. A summary of the rejection

The Action also rejects claims 28, 38-40, 42, and 45-47 under 35 U.S.C. § 102(b) as being anticipated by Maneta-Peyret *et al.* (Maneta-Peyret). Specifically, the Action takes the position that Maneta-Peyret discloses a mixture having PS and cytochrome C. Similar to the

rejection made in reference to Tamamura, the Action concludes that the PS and cytochrome C in the Maneta-Peyret mixture are "conjugate[d]" together.

Applicant traverses this rejection. Claims 28 38-40, 42, and 45-47 are not anticipated by Maneta-Peyret.

ii. Maneta-Peyret does not teach or suggest a phosphatidylserine/polypeptide conjugate composition wherein the phosphatidylserine is covalently coupled to the polypeptide

In contrast to Applicant's claimed invention, and as admitted by the Action, Maneta-Peyret discloses a mixture having PS and cytochrome c. *See* Maneta-Peyret, page 124, column 2. Maneta-Peyret does not appear to include any teachings of covalently coupling the PS with the cytochrome c. In fact, the Action appears to admit this much. *See* the Action, page 4.

Because this reference fails to teach or suggest a phosphatidylserine/polypeptide conjugate composition wherein the phosphatidylserine is covalently coupled to the polypeptide, it does not teach every element of the present invention. As such, the present anticipation rejection cannot be maintained.

Accordingly, Applicant requests that the rejection of claims 28 38-40, 42, and 45-47 as being anticipated by Maneta-Peyret be withdrawn.

iii. Maneta-Peyret fails to teach or suggest a method of making a monoclonal antiboby

Claims 41 and 48-54 are further patentable over the Maneta-Peyret reference because this reference fails to teach or suggest a method of making a monoclonal antibody, much less a monoclonal antibody that specifically binds to phosphatidylserine. In Maneta-Peyret, the collaborators produced antisera by injecting a mixture having PS and cytochrome c into rabbits.

See Maneta-Peyret, page 124 and page 126, FIG. 2. As noted above, this procedure does not produce monoclonal antibodies. *See, e.g.*, the specification, page 14, line 16, to page 15, line 10.

By contrast, claims 41 and 48-54 are directed towards methods of producing a monoclonal antibody. Because Maneta-Peyret does not teach or suggest the use of producing a monoclonal antibody, claims 41 and 48-54 are further not anticipated by this reference.

D. Conclusion

Applicant believes that the present document is a full and complete response to the Office Action dated August 27, 2003. In conclusion, Applicant submits that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested.

The Examiner is invited to contact the undersigned Attorney at (512) 536-3020 with any questions, comments or suggestions relating to the referenced patent application.